WHAT IS CLAIMED

1. A method of making a chimeric mouse, comprising:

a. creating an immunetolerant mouse which has a degenerated liver; and

b. transplanting xenogenic mammalian hepatocytes capable of being infected with at least one compatible mammalian hepatitis virus to repopulate the parenchyma of the degenerated liver.

2. The method of claim 1, which comprises infecting the xenogenic mammalian hepatocytes with hepatitis virus prior to said transplanting.

3. The method of claim 1, which comprises infecting the xenogenic mammalian hepatocytes with hepatitis virus following said repopulation.

4. The method of claim 1, which comprises selecting the xenogenic mammalian hepatocytes from the group consisting of human, chimpanzee, baboon, wooly monkey, ground squirrel, and woodchuck hepatocytes.

5. The method of claim 1, wherein the compatible mammalian hepatitis virus is at least one of a compatible mammalian hepatitis A virus, hepatitis C virus, hepatitis D virus coinfected with hepadnavirus, hepatitis E virus, hepatitis F virus or hepadnavirus.

6. The method of claim 1, wherein the immunetolerant mouse which has a degenerated liver is created by:

a. crossing a hemizygous or homozygous urokinase-type plasminogen activator (uPA) transgenic mouse with a homozygous Recombination Activation Gene 2 (RAG-2)

knockout mouse to generate F1 uPA hemizygous, RAG-2 hemizygous sibling mice; and

b. crossing the F1 mouse to another sibling F1 mouse or to a RAG2 homozygous mouse to generate a uPA hemizygous or homozygous, RAG2 homozygous (uPA/RAG2) F2 mouse.

7. The method of claim 6, wherein the xenogenic mammalian hepatocyte is from a woodchuck and the compatible mammalian hepatitis virus is Woodchuck Hepatitis Virus (WHV).

8. A chimeric mouse model system for hepatitis comprising an immunetolerant mouse having a degenerated liver parenchyma repopulated with transplanted xenogenic mammalian hepatocytes that are capable of being infected with a compatible mammalian hepatitis virus.

9. The chimeric mouse model system of claim 8, wherein the xenogenic mammalian hepatocytes are infected with hepatitis virus prior to said transplantation.

10. The chimeric mouse model system of claim 8, wherein the xenogenic mammalian hepatocytes are infected with hepatitis virus following said repopulation.

11. The chimeric mouse model system of claim 8, wherein the xenogenic mammalian hepatocytes is a member selected from the group consisting of human, chimpanzee, baboon, wooly monkey, ground squirrel, and woodchuck hepatocytes.

12. The chimeric mouse model system of claim 8, wherein the compatible mammalian hepatitis virus is at least one of a compatible mammalian hepatitis A virus, hepatitis C virus, hepatitis D virus coinfected with hepadnavirus, hepatitis E virus, hepatitis F virus or hepadnavirus.

13. The chimeric mouse model system of claim 8, wherein the immunetolerant mouse having degenerated liver parenchyma is hemizygous or homozygous for the urokinase-type plasminogen activator (uPA) transgene and is homozygous for the Recombination Activation Gene 2 (RAG-2) knockout gene.

14. The chimeric mouse model system of claim 13, wherein the xenogenic mammalian hepatocyte is derived from a woodchuck and the compatible mammalian hepatitis virus is Woodchuck Hepatitis Virus (WHV).

15. A method for screening a test compound for anti-viral activity, comprising:

a. administering said test compound to an immunetolerant chimeric mouse which has a degenerated liver parenchyma repopulated with transplanted xenogenic mammalian hepatocytes and wherein the xenogenic mammalian hepatocyes are infected with at least one compatible mammalian virus; and

b. assaying the level of replication of the virus.

16. The method of claim 15, wherein the mammalian virus is at least one hepatitis virus.

17. The method of claim 15, which comprises comparing the level of viral replication in said mouse and in a control mouse which has not been administered the test compound.

18. The method of claim 15, which comprises infecting the xenogenic mammalian hepatocytes with the compatible mammalian virus prior to said transplanting.

19. The method of claim 16, which comprises infecting the xenogenic mammalian hepatocytes with the

compatible mammalian virus following said repopulating step.

20. The method of claim 15, which comprises selecting the xenogenic mammalian hepatocyte from the group consisting of human, chimpanzee, baboon, wooly monkey, ground squirrel, and woodchuck hepatocytes.

21. The method of claim 15, wherein the compatible mammalian virus is at least one of a compatible mammalian hepatitis A virus, hepatitis C virus, hepatitis D virus coinfected with hepadnavirus, hepatitis E virus, hepatitis F virus or hepadnavirus.

22. The method of claim 15, wherein the immunetolerant mouse which has a degenerated liver is hemizygous or homozygous for the urokinase-type plasminogen activator (uPA) transgene and homozygous for the Recombination Activation Gene 2 (RAG-2) knockout gene.

Sub C4 23. The method of claim 22, ~~wherein the xenogenic mammalian hepatocyte is derived from a woodchuck and the compatible mammalian hepatitis virus is Woodchuck Hepatitis Virus (WHV).~~

24. The method of claim 15, wherein the antiviral compound is a member selected from the group consisting of interferons, cytokines, interleukins, growth factors, hormones, nucleoside analogues, and antisense DNA/RNA.

Sub D4 C5 25. A method for screening a test compound for ~~anti-~~ cancer activity, comprising:

a. administering ~~said~~ test compound to an immunetolerant chimeric mouse which has degenerated liver parenchyma repopulated with transplanted xenogenic mammalian hepatocytes and wherein the xenogenic mammalian hepatocyes are

infected with at least one compatible mammalian hepatitis virus; and

b. assaying the mice for the development of hepatocellular carcinoma in said mice.

26. The method of claim 25, which comprises comparing the presence of unique viral DNA integrations in the liver of said mouse and in a control mouse which has not been administered the test compound.

27. The method of claim 25, wherein the chimeric mouse has precancerous or malignant cancerous hepatic tissue and wherein the development of hepatocellular carcinomas is assayed by monitoring for the prevention of the development of cancerous tissue from precancerous tissue or the amelioration of the malignant cancerous tissue.

28. The method of claim 27, which comprises comparing the assay in the chimeric mouse with the same assay carried out in a control mouse which has not been administered the test compound.

29. The method of claim 25, which comprises infecting the xenogenic mammalian hepatocytes with a hepatitis virus prior to said transplantation step.

30. The method of claim 25, which comprises infecting the xenogenic mammalian hepatocytes with hepatitis virus prior to said transplanting step.

31. The method of claim 25, which comprises infecting the xenogenic mammalian hepatocytes are infected with hepatitis virus following said repopulating step.

32. The method of claim 25, which comprises

selecting the xenogenic mammalian hepatocyte from the group consisting of human, chimpanzee, baboon, wooly monkey, ground squirrels and woodchuck hepatocytes.

33. The method of claim 25, wherein the compatible mammalian hepatitis virus is at least one of a compatible mammalian hepatitis A virus, hepatitis C virus, hepatitis D virus coinfected with hepadnavirus, hepatitis E virus, hepatitis F virus or hepadnavirus.

34. The method of claim 25, wherein the immunetolerant mouse which has a degenerated liver is hemizygous or homozygous for the urokinase-type plasminogen activator (uPA) transgene and homozygous for the Recombination Activation Gene 2 (RAG-2) knockout gene.

35. The method of claim 33, wherein the xenogenic mammalian hepatocyte is derived from a woodchuck and the compatible mammalian hepatitis virus is Woodchuck Hepatitis Virus (WHV).

36. The method of claim 25, wherein the anticancer compound is a member selected from the group consisting of interferons, cytokines, interleukins, growth factors, hormones, nucleoside analogues, and antisense DNA/RNA.